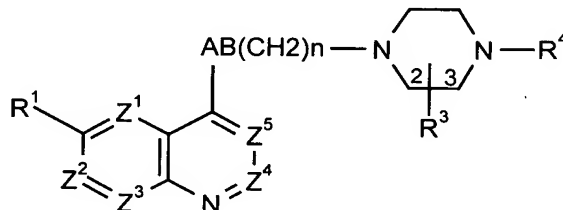


Amendments to the Specification:

Please amend the specification by replacing the paragraph sections under the heading "Related Applications" with the following new paragraph sections:

At page 1, lines 11-20:

This invention provides a compound of formula (I) or a pharmaceutically acceptable ~~derivative~~ **salt and/or N-oxide** thereof:



(I)

wherein:

one of Z¹, Z², Z³, Z⁴ and Z⁵ is N, one is CR^{1a} and the remainder are CH, or one of Z¹, Z², Z³, Z⁴ and Z⁵ is CR^{1a} and the remainder are CH;

At page 2, lines 2-37 to page 3, lines 1-4:

R³ is in the 2- or 3-position and is:

carboxy; (C₁₋₆)alkoxycarbonyl; aminocarbonyl wherein the amino group is optionally substituted by hydroxy, (C₁₋₆)alkyl, hydroxy(C₁₋₆)alkyl, aminocarbonyl(C₁₋₆)alkyl, (C₂₋₆)alkenyl, (C₁₋₆)alkylsulphonyl, trifluoromethylsulphonyl, (C₁₋₆)alkenylsulphonyl, (C₁₋₆)alkoxycarbonyl, (C₁₋₆)alkylcarbonyl, (C₂₋₆)alkenyloxycarbonyl or (C₂₋₆)alkenylcarbonyl and optionally further substituted by (C₁₋₆)alkyl, hydroxy(C₁₋₆)alkyl, aminocarbonyl(C₁₋₆)alkyl or (C₂₋₆)alkenyl; cyano; tetrazolyl; 2-oxo-oxazolidinyl optionally substituted by R¹⁰; 3-hydroxy-3-cyclobutene-1,2-dione-4-yl; 2,4-thiazolidinedione-5-yl; tetrazol-5-ylaminocarbonyl; 1,2,4-triazol-5-yl optionally substituted by R¹⁰; or 5-oxo-1,2,4-oxadiazol-3-yl; or

R³ is in the 2- or 3-position and is (C₁₋₄)alkyl or ethenyl **optionally** substituted with any of the groups listed above for R³ and/or 0 to 3 groups R¹² independently selected from:

thiol; halogen; (C₁₋₆)alkylthio; trifluoromethyl; azido; (C₁₋₆)alkoxycarbonyl; (C₁₋₆)alkylcarbonyl; (C₂₋₆)alkenyloxycarbonyl; (C₂₋₆)alkenylcarbonyl; hydroxy optionally substituted by (C₁₋₆)alkyl, (C₂₋₆)alkenyl, (C₁₋₆)alkoxycarbonyl, (C₁₋₆)alkylcarbonyl, (C₂₋₆)alkenyloxycarbonyl, (C₂₋₆)alkenylcarbonyl or aminocarbonyl wherein the amino group is optionally substituted by (C₁₋₆)alkyl, (C₂₋₆)alkenyl, (C₁₋₆)alkylcarbonyl or (C₂₋₆)alkenylcarbonyl; amino optionally mono- or disubstituted by (C₁₋₆)alkoxycarbonyl, (C₁₋₆)alkylcarbonyl, (C₂₋₆)alkenyloxycarbonyl, (C₂₋₆)alkenylcarbonyl, (C₁₋₆)alkyl, (C₂₋₆)alkenyl, (C₁₋₆)alkylsulphonyl, (C₂₋₆)alkenylsulphonyl or aminocarbonyl wherein the amino group is optionally substituted by (C₁₋₆)alkyl or (C₂₋₆)alkenyl; aminocarbonyl wherein the amino group is optionally substituted by (C₁₋₆)alkyl, hydroxy(C₁₋₆)alkyl, aminocarbonyl(C₁₋₆)alkyl, (C₂₋₆)alkenyl, (C₁₋₆)alkoxycarbonyl, (C₁₋₆)alkylcarbonyl, (C₂₋₆)alkenyloxycarbonyl or (C₂₋₆)alkenylcarbonyl and optionally further substituted by (C₁₋₆)alkyl, hydroxy(C₁₋₆)alkyl, aminocarbonyl(C₁₋₆)alkyl or (C₂₋₆)alkenyl; oxo; (C₁₋₆)alkylsulphonyl; (C₂₋₆)alkenylsulphonyl; or (C₁₋₆)aminosulphonyl wherein the amino group is optionally substituted by (C₁₋₆)alkyl or (C₂₋₆)alkenyl;
provided that when R³ is disubstituted with hydroxy or amino and carboxy containing substituents these may optionally together form a cyclic ester or amide linkage, respectively;

wherein R¹⁰ is selected from (C₁₋₄)alkyl; (C₂₋₄)alkenyl; aryl; a group R¹² as defined above; carboxy; aminocarbonyl wherein the amino group is optionally substituted by hydroxy, (C₁₋₆)alkyl, (C₂₋₆)alkenyl, (C₁₋₆)alkylsulphonyl, trifluoromethylsulphonyl, (C₁₋₆)alkenylsulphonyl, (C₁₋₆)alkoxycarbonyl, (C₁₋₆)alkylcarbonyl, (C₂₋₆)alkenyloxycarbonyl or (C₂₋₆)alkenylcarbonyl and optionally further substituted by (C₁₋₆)alkyl or (C₂₋₆)alkenyl; cyano; or tetrazolyl;

At page 3, lines 19-34:

AB is NR¹¹CO, CO-CR⁸R⁹ or CR⁶R⁷-CR⁸R⁹ or when n is 1 or 2, AB may instead be O-CR⁸R⁹ or NR¹¹-CR⁸R⁹, or when n is 2 AB may instead be CR⁶R⁷-NR¹¹ or CR⁶R⁷-O, provided that when n is 0, B is not CH(OH),

and wherein:

each of R⁶ and R⁷, R⁸ and R⁹ is independently selected from: H; thiol; (C₁₋₆)alkylthio; halo; trifluoromethyl; azido; (C₁₋₆)alkyl; (C₂₋₆)alkenyl; (C₁₋₆)alkoxycarbonyl; (C₁₋₆)alkylcarbonyl; (C₂₋₆)alkenyloxycarbonyl; (C₂₋₆)alkenylcarbonyl; hydroxy, amino or aminocarbonyl optionally substituted as for corresponding substituents in R³; (C₁₋₆)alkylsulphonyl; (C₂₋₆)alkenylsulphonyl; or (C₁₋₆)aminosulphonyl wherein the amino group is optionally substituted by (C₁₋₆)alkyl or (C₁₋₆)alkenyl;
or R⁶ and R⁸ together represent a bond and R⁷ and R⁹ are as above defined;
and each R¹¹ is independently H, trifluoromethyl, (C₁₋₆)alkyl, (C₁₂₋₆)alkenyl, (C₁₋₆)alkoxycarbonyl, (C₁₋₆)alkylcarbonyl, aminocarbonyl wherein the amino group is optionally substituted by (C₁₋₆)alkoxycarbonyl, (C₁₋₆)alkylcarbonyl, (C₁₂₋₆)alkenyloxycarbonyl, (C₂₋₆)alkenylcarbonyl, (C₁₋₆)alkyl or (C₁₂₋₆)alkenyl and optionally further substituted by (C₁₋₆)alkyl or (C₁₂₋₆)alkenyl;
or where one of R³ and R⁶, R⁷, R⁸ or R⁹ contains a carboxy group and the other contains a hydroxy or amino group they may together form a cyclic ester or amide linkage

wherein:

'heterocyclic' is an aromatic and non-aromatic, single or fused, ring containing up to four hetero-atoms in each ring selected from oxygen, nitrogen and sulphur, and having from 4 to 7 ring atoms, which rings may be unsubstituted or substituted by up to three groups selected from amino, halogen, (C₁₋₆)alkyl, (C₁₋₆)alkoxy, halo(C₁₋₆)alkyl, hydroxy, carboxy, carboxy salts, (C₁₋₆)alkoxycarbonyl, (C₁₋₆)alkoxycarbonyl(C₁₋₆)alkyl, aryl, and oxo groups, and wherein any amino group forming part of a single or fused non-aromatic heterocyclic ring as defined above is optionally substituted by (C₁₋₆)alkyl optionally substituted by hydroxy, (C₁₋₆)alkoxy, thiol, (C₁₋₆)alkylthio, halo or trifluoromethyl, acyl or (C₁₋₆)alkylsulphonyl groups;

'aryl' is phenyl or naphthyl, optionally substituted with up to five groups selected from halogen, mercapto, (C₁₋₆)alkyl, phenyl, (C₁₋₆)alkoxy, hydroxy(C₁₋₆)alkyl, mercapto (C₁₋₆)alkyl, halo(C₁₋₆)alkyl, hydroxy, amino, nitro, cyano, carboxy, (C₁₋₆)alkylcarbonyloxy, (C₁₋₆)alkoxycarbonyl, formyl and (C₁₋₆)alkylcarbonyl groups;

'acyl' is (C₁₋₆)alkoxycarbonyl, formyl or (C₁₋₆) alkylcarbonyl.

At page 4, lines 1-11:

The invention also provides the use of a compound of formula (I) or a pharmaceutically acceptable **derivative salt and/or N-oxide** thereof in the manufacture of a medicament for use in the treatment of bacterial infections in mammals.

The invention also provides a pharmaceutical composition for use in the treatment of bacterial infections in mammals comprising a compound of formula (I), or a pharmaceutically acceptable **derivative salt and/or N-oxide** thereof, and a pharmaceutically acceptable carrier.

The invention further provides a method of treatment of bacterial infections in mammals, particularly in man, which method comprises the administration to a mammal in need of such treatment of an effective amount of a ~~a~~ compound of formula (I), or a pharmaceutically acceptable **derivative salt and/or N-oxide** thereof.

At page 4, after line 14 and before lines 15-20:

Preferably one of Z¹, Z², Z³, Z⁴ and Z⁵ is N and one of Z³ and Z⁵ if not N is CR^{1a} and the remainder are CH, or one of Z¹, Z², Z³, Z⁴ and Z⁵ is CR^{1a} and the remainder are CH.

More preferably Z⁵ is CH or N, Z³ is CH or CF and Z¹, Z² and Z⁴ are each CH, or Z¹ is N, Z³ is CH or CF and Z², Z⁴ and Z⁵ are each CH. Most preferably Z¹-Z⁵ are each CH.

At page 4, lines 26-37:

In one aspect, R³ is preferably hydrogen, (C₁₋₄) alkyl, ethenyl, **or 1-hydroxy-(C₁₋₄) alkyl** optionally substituted **1-hydroxy-(C₁₋₄) alkyl as defined in formula (I)**, more preferably hydroxymethyl, 1,2-dihydroxy(C₂₋₄)alkyl wherein the 2-hydroxy group is optionally substituted **as defined in formula (I)**. Preferred examples of R³ include hydroxymethyl, 1-hydroxyethyl or 1,2-dihydroxyethyl wherein the 2-hydroxy group is optionally substituted with alkylcarbonyl or aminocarbonyl where the amino group is optionally substituted **as defined in formula (I)**. Other suitable examples of R³ include 2-hydroxyethyl, 2- or 3-hydroxypropyl, ethyl or ethenyl.

In another aspect R³ preferably contains carboxy, **aminocarbonyl** optionally substituted **aminocarbonyl, as defined in formula (I)**, cyano or 2-oxo-oxazolidinyl optionally substituted by R¹⁰. Where R³ is substituted alkyl is it preferably substituted methyl. Preferred examples of R³ include CO₂H, CH₂CO₂H,

$(\text{CH}_2)_2\text{CO}_2\text{H}$, $(\text{CH}_2)_2\text{CN}$, $\text{CH}(\text{OH})\text{CH}_2\text{CN}$, $\text{CH}(\text{OH})\text{CH}_2\text{CO}_2\text{H}$, $\text{CH}=\text{CHCO}_2\text{H}$ or 2-oxo-oxazolidinyl.

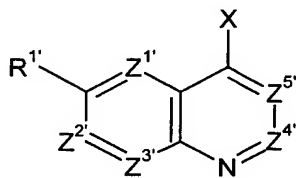
At page 6, lines 12-13:

The term 'acyl' includes (C_{2-6}) alkoxycarbonyl, formyl or (C_{2-6}) alkylcarbonyl group. **Aryl are preferably substituted with up to three groups.**

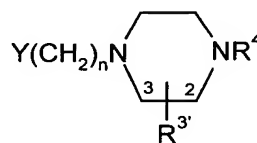
At page 7, lines 1-33 to page 8, lines 1-11:

In a further aspect of the invention there is provided a process for preparing compounds of formula (I), or a pharmaceutically acceptable **derivative salt and/or N-oxide** thereof, which process comprises:

(a) reacting a compound of formula (IV) with a compound of formula (V):



(IV)



(V)

wherein Z^1 , Z^2 , Z^3 , Z^4 and Z^5 , m , n , R^1 , R^3 and R^4 are as defined in formula (I), and X and Y may be the following combinations:

- (i) X is M and Y is $\text{CH}_2\text{CO}_2R^X$, CH_2CHO or CH_2COW
- (ii) X is CO_2R^Y and Y is $\text{CH}_2\text{CO}_2R^X$
- (iii) one of X and Y is $\text{CH}=\text{SPh}_2$ and the other is CHO
- (iv) X is CH_3 and Y is CHO
- (v) X is CH_3 and Y is CO_2R^X
- (vi) X is $\text{CH}_2\text{CO}_2R^Y$ and Y is CO_2R^X
- (vii) X is $\text{CH}=\text{PR}^{Z_3}$ and Y is CHO
- (viii) X is CHO and Y is $\text{CH}=\text{PR}^{Z_3}$
- (ix) X is halogen and Y is $\text{CH}=\text{CH}_2$
- (x) one of X and Y is COW and the other is $\text{NHR}^{11'}$ ~~or NCO~~
- (xi) one of X and Y is $(\text{CH}_2)_p\text{-W}$ and the other is $(\text{CH}_2)_q\text{NHR}^{11'}$ or $(\text{CH}_2)_q\text{OH}$
- (xii) one of X and Y is CHO and the other is $\text{NHR}^{11'}$,

or where $n=0$

(xiii) X is A-B-(CH₂)_n-W or A-B-(CH₂)_{n-1}-CHO and Y is H

(xiv) X is NCO and Y is H

(xv) X is CH₃ and Y is H

(xvi) X is COCH₂W and Y is H

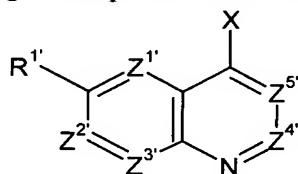
(xvii) X is CH=CH₂ and Y is H

(xviii) X is oxirane and Y is H

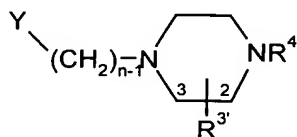
in which W is a leaving group, R^x and R^y are (C₁₋₆)alkyl and R^z is aryl or (C₁₋₆)alkyl;

or

(b) reacting a compound of formula (IV) with a compound of formula (Vb):



(IV)



(Vb)

wherein Z¹, Z², Z³, Z⁴ and Z⁵, m, n, R¹, R³ and R⁴ are as defined in formula (I), X is CH₂NHR^{11'} and Y is CHO or COW;

in which Z^{1'}, Z^{2'}, Z^{3'}, Z^{4'}, Z^{5'}, R^{11'}, R^{1'}, R^{3'} and R^{4'} are Z¹, Z², Z³, Z⁴, Z⁵, R¹¹, R¹, R³ and R⁴ or groups convertible thereto, and thereafter optionally or as necessary converting Z^{1'}, Z^{2'}, Z^{3'}, Z^{4'}, Z^{5'}, R^{11'}, R^{1'}, R^{3'} and R^{4'} to Z¹, Z², Z³, Z⁴, Z⁵, R¹¹, R¹, R³ and R⁴, converting A-B to other A-B, interconverting Z¹, Z², Z³, Z⁴, Z⁵, R¹¹, R¹, R³ and/or R⁴ and forming a pharmaceutically acceptable **derivative salt and/or N-oxide** thereof.

At page 20, lines 31-33:

No toxicological effects are indicated when a compound of formula (I) or a pharmaceutically acceptable salt ~~or in vivo hydrolysable~~ **and/or N-oxide** thereof is administered in the above-mentioned dosage range.